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| 10/029,654 | 12/21/2001 | Birgit Jung | I/1178 | 7012 |
| 28501 | 7590 | 03/04/2004 | EXAMINER | |
| BOEHRINGER INGELHEIM CORPORATION 900 RIDGEBURY ROAD P. O. BOX 368 RIDGEFIELD, CT 06877 | | | SAUNDERS, DAVID A | |
| | | | ART UNIT | PAPER NUMBER |
| | | | 1644 | |

DATE MAILED: 03/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

029,654

Applicant(s)

JUNG et al

Examiner

SAUNDERS

Group Art Unit

1644

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

- ☒ Responsive to communication(s) filed on 11/24/03
- ☐ This action is **FINAL**.
- ☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- ☒ Claim(s) 1, 3-4, 7-13, 21-29 is/are pending in the application.
- Of the above claim(s) 21-29 is/are withdrawn from consideration.
- ☒ Claim(s) 9-13 is/are allowed.
- ☒ Claim(s) 1, 3-4, 7-8 is/are rejected.
- ☐ Claim(s) _____ is/are objected to.
- ☒ Claim(s) 1, 3-4, 7-13, 21-29 are subject to restriction or election requirement.

Application Papers

- ☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- ☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
- ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

- ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
 - ☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been received.
 - ☐ received in Application No. (Series Code/Serial Number) _____
 - ☐ received in this national stage application from the International Bureau (PCT Rule 1.7.2(a)).

*Certified copies not received: _____

Attachment(s)

- ☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
- ☒ Notice of Reference(s) Cited, PTO-892
- ☐ Notice of Draftsperson's Patent Drawing Review, PTO-948
- ☐ Interview Summary, PTO-413
- ☐ Notice of Informal Patent Application, PTO-152
- ☐ Other _____

Office Action Summary

The amendment of 11/24/03 has been entered. Claims 1, 3-4, 7-13 and 21-29 are pending.

Applicant's election with traverse of Group III (claims 1-4 and 7-8) in Paper No. whatever filed on 11/24/03 is acknowledged. The traversal is on the ground(s) that there would be no undue burden in searching all groups that pertain to ARL4 expression, activation and inhibition. This is not found persuasive because the argument that there would be no undue burden in the search would be only applicable to the claims of Group X (claims 9-13, which have steps/features in common with those of claim 1). As for the claims of Groups X XIV and X X X I , examination of these would involve an undue search burden. Since these would involve use of a genus substances which have only been described functionally, and which, therefore, have not been properly described under 35 USC 112, first paragraph; the claims are unsearchable.

The claims under examination are thus those of Groups III and X (claims 1, 3-4 and 7-13).

The requirement is still deemed proper and is therefore made FINAL.

The disclosure is objected to because of the following informalities: at page 5, line 7 "1985-1902" is erroneous, since the starting page of the reference is higher numbered than the ending page.

Appropriate correction is required.

Claims 1, 3-4 and 7-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is unclear as to whether or not the method is performed with a test system that includes a hyperactivated macrophage. The preamble and step (b) refer to such a macrophage. Dependent claim 7 requires a cellular system, for which it is not clear as to whether this has macrophages or some other kind of cells. Dependent claim 8 requires a cell-free system; if base claim 1, employs a test system with hyperactivated macrophages, how can one then have a cell-free embodiment in claim 8?

In claims 3 and 4 the terms "directly" and "indirectly" are not clear, since the specification does not define these, it is not clear how far removed (e.g. in terms of metabolic steps or of cascading activation steps) the measured read-out may be from the function of ARL4 per se.

Claims are unclear as to what constitutes a "measurable read-out." Claim 1 part (a) refers to this as a "biological function of ARL4," while dependent claims 3 and 4 more generically measure the "inflammatory process."

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Peterson et al (5,883,084).

Peterson et al teach that it is of interest to reduce the inflammatory activity of alveolar macrophages in respiratory diseases such as COPD. See col. 1, lines 1-30 and col.8, lines 53-56. In Example 1 (cols. 4-5) they show a test for the ability of a test compound (CPR 2001) to inhibit the inflammatory activity of macrophages. The read out is measured in terms of the amount of reactive oxygen species released, compared against control level.

This example is considered consistent with instant claims 1 and 4, since the production of reactive oxygen species may be properly considered as an end –event in a series of cascading events that occur during macrophage activation. Because applicant has not defined what ARL4 precisely accomplishes during activation and because applicant has not defined precisely what is meant by “indirectly” in claim 4, it is taken that a system employing the production of reactive oxygen species as the read-out properly anticipates. Because the ARL4 protein and others identified by applicant would such be involved in a cascading series of activation steps, that can cross-modulate at various points and that can lead to the end result of the production of reactive oxygen species (ROS), it is taken that measurement of ROS levels serves as an “indirect” measure of a biological function of ARL4.

Furthermore, since claim 4 merely requires a measurement of “the inflammatory process” in general terms, the determination of ROS production by Peterson et al meets the limits of the claim.

Claim 7 is rejected since the test system of Peterson et al uses cultured cells.

Claims 1, 4 and 7-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Fuhrman et al (5,470,885).

Fuhrman et al show a test system involving use of activated alveolar macrophages and a test compound (PFOB). The read-out is in terms of peroxide and free radical (FR) production. Read-out in the presence of the test compound is compared against the read-out in the absence thereof to show that the test compound inhibits peroxide and FR production. See example 4 at col.8.

Production of peroxides and free radicals is taken to be an end event of a series of activation steps in the activation of alveolar macrophages. See col.1, lines 10-29 anticipation is stated on the basis that measurement of peroxide and FR production serves as an "indirect" read-out of ARL4 function.

Claim 7 is rejected since Example 4 uses macrophage cells at a first stage involving incubation with the test compound. Claim 8 is rejected, since the read-out assays were performed thereafter on "cell-free supernatants." Applicant's disclosure has given no definitions of "cellular" and "cell-free" systems in terms of what stage(s) of the method are defined as such. Therefore any method which has both a "cellular" and a "cell-free" stage can be properly considered to be consistent with both claims 7 and 8.

The following art is cited as of interest: Murray et al 2003/0049 722 teach expressed gene profiles of activated/destructive macrophages. The teach use of the encoded proteins in drug screening assays. They teach measuring the levels of such proteins in diagnostic assays.

Instant claims 9-13 are allowable over the prior art of record. These claims recite "determining the level of ARL4." This is taken to mean that the level of ARL4 per se is measured, rather than the function of some other protein that is indirectly modulated/activated in its function as a result of ARL4. If applicant does not concur with this interpretation of the claims, prior art may be applied against these claims.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Saunders, PhD whose telephone number is 571-272-0849. The examiner can normally be reached on Monday-Thursday from 8:00 a.m to 5:30 p.m. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached on 571-272-0841.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Saunders/tgd

February 23, 2004


DAVID SAUNDERS
PRIMARY EXAMINER
ART UNIT 182-1644